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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/125,747	08/25/1998	FERNAND NARBEY TOROSSIAN	TORO-0101-PU	8139

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EXAMINER	
SHAHNAN SHAH, KHATOL S	
ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 02/07/2003 28

Please find below and/or attached an Office communication concerning this application or proceeding.

	Application No.	Applicant(s)	
Office Action Summary	09/125,747	TOROSSIAN, FERNAND NARBEY	
	Examiner	Art Unit	
	Khatol S Shahnan-Shah	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 October 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *17-28* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *17-28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Acknowledgement is made of Applicant's response and amendment F filed 10/15/2002 paper number 27.

2. Claims 9-16 were canceled. Claims 17, 18, 23 and 24 were amended. Specification page 13, lines 4-6 was amended. Applicant recited on page 2 of the amendment that claim 28 was amended too, however no amendment was made to claim 28 by the applicant.

3. Claims 17-28 are pending and under consideration.

Prior Citations of Title 35 Sections

4. The text of those sections of Title 35 U.S. Code not included in this action can be found in a prior office action.

Prior Citations of References

5. The references cited or used as prior art in support of one or more rejections in the instant office action have been previously cited and made of record. No form PTO-892 or form PTO-1449 have submitted with this office action.

Objections Withdrawn

6. Objection to claims 17, 23 and 24 made in paragraph 6 of the office action mailed April 08, 2002 (paper number 25) is withdrawn in view of the applicant's amendments of the claims.

Objections Maintained

7. Objections to the specification made in paragraph 5 of the office action mailed April 08, 2002 (paper number 25) are maintained. However applicant's response of 10/15/2002 has been noted that the square brackets will be removed at a later date.

Rejections Moot

8. The rejection of claims 9-16 under 35 USC § 112, First Paragraph made in paragraph 7 of the office action mailed 08/ 28/ 2001 (paper # 23) is moot in view of applicant's cancellation of those claims.

9. The rejection of claims 9-16 under 35 USC § 112, first Paragraph made in paragraph 7 of the office action mailed April 08, 2002 (paper number 25) is moot in view of applicant's cancellation of those claims.

Rejections Withdrawn

10. The rejection of claims 9-28 under 35 USC § 112, second Paragraph made in paragraph 8 of the office action mailed April 08, 2002 (paper number 25) is withdrawn in view of the applicant's amendments of the claims.

Rejections Maintained

11. The rejection of claims 17-28 under 35 USC § 112, first Paragraph made in paragraph 7 of the office action mailed April 08, 2002 (paper number 25) is maintained.

Applicant's arguments filed 10/15/2002 have been fully considered but they are not persuasive.

Applicant argue " The Examiner objected to the claims under 112 on the basis that there was insufficient evidence that the claimed vaccine is capable of inducing immunity against *Helicobacter* infection, for the reason that the experiments did not demonstrate an " art recognized standard" of improvement over the control of the efficacy of the vaccines. That ground of objection is not correct, however, since successful results obtained with the claimed

vaccine are illustrated in the four examples set forth in the specification (pages 22-24). Applicant further provides Exhibits A, B and C as updated relevant publications.

It is the examiner's position that the examples set forth in the specification (pages 22-24) fail to set forth sufficient evidence showing that the claimed vaccine complex could be effective in treating or preventing disease or how it can be made. No guidance has been provided as to their source and as to how they are produced.

Claim 19, which depends from claim 17, recites the immunomodulatory and vaccine complex of the instant invention for use in the treatment of diseases caused by *Helicobacter* bacteria "by the production of antibodies". However, the specification on page 3, lines 3 and 4, states the "inefficacy" of the *Helicobacter*-specific antibodies in protecting an individual.

Furthermore, pages 12 and 13 of the specification recite collagen type III as the "immunity adjuvant factor", and the complex as containing "amino acid" of the collagen type III. The collagen type III listed on Swiss-Prot. from Human or Bovine proteins contain at least 1466 and 1049 amino acids. (See attached data). However, claim 18 recites that the amino acids from collagen are selected from the various amino acids recited in the claim. Claim 18 recites, " wherein the type III collagen comprises amino acids selected from the group consisting of.....and mixtures thereof. " It is unclear what Applicant means by this recitation. Is type III collagen only made of a single amino acid recited in the group?

With this description, one of [redacted] skill in the art would not be able to understand whether the whole sequence is present in the complex, or any one of the recited amino acids is included in the complex, or a mixture of any of these amino acids is included in the complex, and therefore would not be able to make and/or use and/or reproducibly practice the invention without undue

experimentation. On page 14 of the specification, it is stated that the vaccine complex of the invention is produced by " combining ribosomal RNAs or RNA fragments, membrane fractions (for example proteoglycans from *Klebsiella pneumoniae*) and collagen type III...." To obtain a high level of protection and cure". Neither the source of ribosomal RNAs, RNA fragments, or the recited collagen, nor the nature of the antibiotic resistant disease or the antibiotic resistant bacteria against which it supposedly produces high level cure or protection is described.

Further, the specification does not allow one of [redacted] skill in the art to grasp the nature of the association between the multiple components present in the "complex". For example, the optimal amounts or proportions of different "bacterial membrane fractions", i.e., glycopeptides and/or lipopolysaccharides and the ribonucleic acid arm, that should be present in the complex such that the complex can accomplish its alleged therapeutic and/or preventive functions are not disclosed.

In regards to applicants' Exhibits. It is the examiner' position that applicants have provided exhibit A as a good review article for diagnosis of *Helicobacter pylori* discussing large battery of methods including UBT and serology. But endoscopy and evaluation of tissue samples is still the art-recognized gold standard for diagnosis of *Helicobacter pylori* (see applicants exhibit A, page 124 last three paragraphs).

Using exhibit B applicants try to argue why they did not provide animal data. Applicants further argue because of lack of animal model the therapeutic effect of the claimed complex was tested in humans, and the examples in pages 22-24 illustrate the results of those tests.

It is the examiner's position that the examples set forth in the specification (pages 22-24)

fail to set forth sufficient evidence showing that the claimed vaccine complex could be effective in treating or preventing disease or how it can be made. No guidance has been provided as to their source and as to how they are produced. Furthermore Rappouli R. et al. (applicants exhibit B, page 9) recite "It is thus evident that, to be efficacious, vaccine must induce immune responses that protective in both quantitative and qualitative terms, without triggering un wanted side effects". In the present disclosure applicants' specification is completely silent about these facts.

Applicants further refer to exhibit C as Journal of Physiology and Pharmacology 48 Suppl.4: 59-65 1997. The applicants did not submit this article. What applicants submitted as exhibit C was few pages including contents and cover of *Helicobacter pylori* Basic mechanisms to Clinical Cure 2000.

In summary, the actual invention is not described in such a way that one skilled in the art could grasp the invention and make and/or use the invention and/or reproducibly practice the invention with a reasonable expectation of success, without undue experimentation. The breadth of instant claims is not commensurate in scope with the enabling disclosure or evidence. In the absence of specific guidance and evidence, instant claims are viewed as not meeting the enablement provisions of 35 U.S.C. § 112, first paragraph.

12. Claims 17-28 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 17 and all its dependent claims recite the term " immunomodulatory". The term is not defined by the claims or the specification. Applicants argued in page 7 of 10/15/2002

amendment that Exhibit A (Dated 2000) explains " immunomodulatory" and the concept is well known to persons of ordinary skill in the art and does not need to be specifically defined. It is the examiner's position the reference used by the applicants has been published 4 years after the invention was made. Therefore the concept was not well known to persons of ordinary skill in the art at the time the invention was made.

Claim 18 recites, " Wherein the type III collagen comprises amino acids selected from the group consisting of.....and mixtures thereof. " It is unclear what Applicant means by this recitation. Is type III collagen only made of a single amino acid recited in the group?

Claim 19 depends from claim 17, the vaccine complex of which comprises of type III collagen and bacterial membrane fractions and ribonucleic acid extracted from selected species of *Helicobacter*. What is the specificity of the antibodies? Are these antibodies specific to all molecules or to the part (b) and (c) components?

Conclusion

13. Claims 17-28 stand rejected.

14. THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37

CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Khatol Shahnan-Shah whose telephone number is (703) 308-8896. The examiner can normally be reached on 7:30 AM - 4 PM from Monday through Friday. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette F Smith, can be reached on (703) 308-3909. The fax phone number for the organization where this application or proceeding is assigned to is (703) 305-3014.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Khatol Shahnan-Shah, BS, Pharm, MS

Biotechnology Patent Examiner

Art Unit 1645

January 26, 2003

LYNETTE F. SMITH
PRIMARY EXAMINER
GROUP ~~1800~~ 1600